Poverty-Related and Neglected Diseases in Horizon 2020 – Gaps and Challenges

The European Commission has proposed to allocate €80 billion to the 2014-2020 Research and Innovation Framework Programme (Horizon 2020). On-going discussions on Horizon 2020 in the Council and European Parliament indicate that there is strong support for investment in research and development (R&D) for Poverty-Related and Neglected Diseases (PRNDs) amongst EU Member States and Members of the European Parliament (MEPs).

However glaring gaps, which would prevent the full PRND R&D cycle being covered, can be identified in the proposals and work plans under discussion. This paper seeks therefore, to highlight some of those gaps and to examine the challenges to ensuring an increased budget that covers the full PRND R&D cycle.

The European Commission's Directorate-General (DG) for Research and Innovation proposes channelling the majority of its PRND R&D funding through the European Research Council (ERC), the Innovative Medicines Initiative (IMI), the European and Developing Countries Clinical Trials Partnership (EDCTP) and research to combat antimicrobial drug resistance (AMDR). Looking at the current agenda of these existing initiatives, it is difficult to see how the full PRND R&D cycle could be covered. In particular, the full product development cycle would need to be addressed, including pre-competitive discovery, pre-clinical research, clinical trials and manufacturing and access, stages which are vital in establishing a constantly replenished product development pipeline.

Furthermore, there are clear signs that calls for proposals will be drafted to focus funding along so-called horizontal lines, such as on vaccines, diagnostics and treatments. This will be a setback compared to the current situation of disease-specific calls for proposals, as PRNDs will be in competition with many non-poverty-related diseases. Strong disease expertise has been established through disease-specific funding; this is pivotal for developing new prevention technologies, diagnostics and treatments, and is a prerequisite for successful horizontal cooperation. If long-term disease-specific funding is not ensured, European researchers might be drawn to different disease areas or research environments where funding flows are more stable.

After considerable investment into R&D for PRNDs over the past ten years, incredible progress has been made in the development of new tools for many PRNDs. We are about ten years away from developing a new tuberculosis (TB) vaccine - an essential tool if we are to eliminate TB as a public health threat. We need sustained public investment if we are to deliver the products we have already invested in, and that have reached advanced stages.

To address these challenges, it is essential that R&D for PRNDs be sustained through specific calls for proposals under Horizon 2020. Horizontal approaches must be coupled with disease-specific approaches to avoid losing the expertise and excellence we have developed over the past decade. Support for translational research and development should be seriously considered to maximise chances of research efforts delivering innovative products to fight PRND's.

European and Developing Countries Clinical Trials Partnership (EDCTP)

- EDCTP has become an extremely successful partnership between the EU, sub-Saharan African partners and third parties (such as private sector entities or public bodies from third countries). The second phase of the partnership **(EDCTP II 2014-2024) is pivotal for advancing global health clinical research,** and the European Commission is to be congratulated for its full support of EDCTP II, including its proposal to expand its scope to post-marketing studies (phase IV studies), diagnostics, neglected infectious diseases, health services research.[1]

However, the overall scope of EDCTP's activities is not all-encompassing:

[1] All statements made in reference to EDCTP II are based on the current state of play. The final design of EDCTP II is subject to discussions among the European Commission, the Council and the European Parliament. A proposal for a Regulation on EDCTP II is expected in early 2012.

- **EDCTP predominantly provides funding for clinical trials in phases II and III, and does not generally invest in earlier trial phases or in operational research.** Hence, incentives for pre-competitive discovery (basic research[2]), pre-clinical research, manufacturing and marketing are not covered. Furthermore, **clinical trials phase I and small scale phase II are only funded in exceptional cases of a lack of alternative funding and where there is strategic and scientific impact**.[3]
- Although EDCTP collaborates in global consortia, **EDCTP focuses specifically on sub-Saharan Africa**. In order to address different disease strains and interventions in countries with exceptionally high incidences of resistant cases, funding is needed to cover clinical trials in other PRND-endemic regions in the world, such as North Africa, Latin America and Asia. This also holds true for EDCTP's involvement in global consortia, such as "Malaria in Pregnancy" and REMox, where support only goes to the participation of sub-Saharan African members.
- In addition to supporting clinical trials, EDCTP focuses on capacity-building to conduct clinical trials and train health researchers and doctors in PRND-endemic countries. While it is planned to involve more researchers, in particular from the so-called 'new' Member States[4], to increase the support for EDCTP II in those countries **European researchers need to be presented with incentives to continue and increase research into PRNDs R&D.**
- Despite expanding its diseases scope, **EDCTP II will most probably not cover all** Neglected Tropical Diseases (NTDs) but rather those NTDs and additional high-burden diseases (e.g. diarrhoeal diseases and pneumonia) of greatest relevance to Sub-Saharan Africa. It is possible that at the early phase of EDCTP II, co-morbidities of HIV & AIDS, malaria and TB as will be prioritised, as these diseases predispose or potentiate one another, or create treatment difficulties by drug-drug interactions.[5]

European Research Council (ERC)

- ERC supports **bottom-up competition** for grants and **does not predetermine specific research subjects**, although the Scientific Council of the ERC pre-determined 25 panels covering all fields of science, technology and scholarship under FP7.
- **Only individual researchers** backed by an academic host institution are eligible to apply for grants[6]. Despite the importance and strong track record of networks for this kind of global public goods research in the EU, networks are not eligible for funding under the ERC granting scheme.
- The only selection **criterion for proposals** is the **potential for fundamental advances at, and beyond, the 'frontier' of knowledge**. The ERC is an instrument of the first pillar of Horizon 2020, which aims at advancing excellence in science in Europe, as opposed to pillar three of Horizon 2020 that is dedicated to Societal Challenges, including infectious diseases. The result is that there is no safeguard mechanism to ensure that basic research is conducted in areas of societal importance such as PRNDs. In fact, grants under the life science panel of **Immunity and Infection**[7] represented only 11 per cent of the overall life science projects from 2007-2011 and **only 4 per cent of all ERC projects funded from 2007-11**.

Innovative Medicines Initiative (IMI)

[2] Under Horizon 2020, basic research is currently expected to be mainly funded under the ERC budget.
[3] EDCTP II Strategic Business Plan: http://www.edctp.org/fileadmin/documents/Towards_EDCTP_II/EDCTP_Strategic_Business_Plan_for_EDCTP-II_-_publication_May_2012.pdf, pg.7.
[4] Bulgaria, Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovakia, Slovenia.
[5] This is subject to approval from the European Parliament and Council in line with the co-decision procedure.
[6] The so-called 'Synergy Grants' given to a group of 2-4 Principal Investigators are in a pilot phase.
[7] The life science panel 'Immunity and Infection' includes not only PRND R&D issues, but also the field of anti-microbial resistance.

- IMI is **Europe's largest public-private partnership funded under FP7. Funding is matched** mainly by in-kind contributions (consisting mostly of research activities) from **member companies of the European Federation of Pharmaceutical Industries and Associations (EFPIA)**.
- IMI **supports pre-competitive collaborative research**, i.e. finding methods for testing and developing new drugs. Actual drug development is outside the scope of IMI's activities.
- IMI's research agenda is proposed by its Scientific Committee, currently made up of 15 scientists and researchers, including representatives from disease or function-specific research bodies and from the pharmaceutical sector.
- **IMI's research agenda heavily focuses on chronic diseases** such as cancer, asthma, respiratory diseases, and diabetes type II as well as diseases with genetic predisposition (autism, Alzheimer's, diabetes type I). These are threats to European public health and, thus, of economic interest to the European pharmaceutical industry.
- Out of 30 projects, **IMI currently only runs two projects with PRND R&D relevance**: PreDiCT-TB[8] **on TB** (€28.6 million and RAPP-ID on the development of point of care diagnostics for infectious diseases (€14.4 million). Together, these correspond to only 7.5 per cent of the total budget for IMI's first three calls for proposals.[9]

Research to combat antimicrobial drug resistance (AMDR)

- **Antimicrobial resistance is a major obstacle to the treatment of infectious diseases worldwide**. Under the EU's 6th and 7th Research Framework Programmes, a wide range of projects were funded focusing on basic research, strategies for the prudent use of existing antimicrobials, development of new antimicrobials, development of point of care diagnostics and vaccine development.
- Although drug resistance of viral, fungal and parasitic infections is not excluded from AMDR topics under FP7, **AMDR of bacterial infections has been the major focus of EU-funded projects** in response to surging incidence of severe hospital and community-acquired bacterial infections in Europe.
- **Only five out of 21 PRNDs are caused by bacteria.[10]** The majority of PRNDs are caused by viruses, parasites or are of other micro-organic aetiology.
- While under FP6 17 PRND specific projects were funded with a total of €39.8 million, representing 22 per cent of all FP6 AMDR, **under FP7 no PRND specific project** has yet been listed.[11] Although the development of new drugs for resistant strains of TB and diagnostics that detect drug-resistance is indeed essential, the most **recent tendency to focus on a limited range of pathogens, mostly bacteria, is unsettling** considering other unmet needs.

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TBVI
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[8] PreDiCT-TB is one of the world's only initiatives focused on tackling pre-clinical research barriers to the discovery and development of new TB drug combinations; funded under IMI's 3rd call for proposals (2010);
[9] IMI's 5th call suggested that a screening platform could be used for neglected diseases - http://www.imi.europa.eu/sites/default/files/uploads/documents/5th_Call/5thCall_Topics_Final.pdf
[10] PRNDs of bacterial origin are: Buruli Ulcer, Leprosy, Trachoma, Tuberculosis and Yaws.
[11] http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/projects_en.html